Please amend claim 48 as follows:

--48. A method for designing a compound capable of binding to the Stem Cell Factor-binding site of a Kit receptor comprising the steps of:

a) determining the 3-D structure of a fragment of Stem Cell Factor (SCF) by computing atomic co-ordinates from X-ray diffraction data of a crystal of the fragment of SCF, wherein the fragment of SCF consists of consecutive amino acids the sequence of which is set forth in SEQ ID NO:1;

b) determining a Kit receptor binding site on the fragment of SCF based on the 3-D structure; and

c) designing a compound capable of binding to the Stem Cell Factor-binding site of the Kit receptor based on a 3-D structure shape complementarity or estimated interaction energy.

A mark-up copy of the amendments to the claims is attached hereto as **Exhibit A**.

REMARKS

Claims 21, 22, 26, 27, and 48 to 51 are pending in the subject application. Applicants have hereinabove canceled claim 49 and amended claim 48. Applicants maintain that the amendments to the claims raise no issue of new matter. Support for amended claim claim 48 can be found in the specification as originally filed, *inter alia*, at page 37, lines 1-13; at page 9, lines 3-5; page 37, lines 15-17; page 10 lines 3-30; and page 10, lines 25-26. Accordingly, applicants respectfully request entry of this Amendment. Upon entry of this Amendment claims 21, 22, 26, 27,

48, 50, and 51 will be pending and under examination.

Claims Rejected Under 37 C.F.R. §112 - First Paragraph

In the March 14, 2003 Final Office Action the Examiner stated that claims 21-22 and 26-27 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for a method of designing a compound binding to kit using the coordinates of SCF fragment crystal consisting of the sequence of SEQ ID NO:1, does not reasonably provide enablement for a method using the coordinates of any SCF fragment or any polypeptide comprising the sequence of SEQ ID NO:1. The Examiner stated that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The Examiner stated that this rejection is reiterated from the previous Office Action and maintained for reasons of record. The Examiner also stated that while the present rejection is a scope of enablement rejection, it is set forth in the previous Office Action.

The Examiner stated that the claims require making crystals and determining the 3-D structure of any fragment of a SCF protein. The Examiner further stated that applicants argue that since the specification provides an example for the fragment of SCF comprising SEQ ID NO:1, those skilled in the art would know how to make crystals of any fragment of SCF for X-ray crystallography is routine, uses extensive automation, and has been an established field for more than 50 years. The Examiner stated that this is not deemed persuasive because, as set forth in the previous Office Action, the field of crystallography is unpredictable, and as such, the specification, which lacks

guidelines to make crystals of any SCF fragment, is not enabling for using each and every crystal structure of the portion/fragment of SCF polypeptide. The Examiner also stated that while there are kits or automated systems for crystallography commercially available, it is well established in the field that the utilization of a variety of crystallization methods including kits, for the protein in question, greatly improves the chances of identifying suitable conditions for crystallization, obtaining suitable single crystal(s) is the least understood step in the X-ray structural analysis of a protein(s). The Examiner stated that, therefore, since the science of protein crystallization is underdeveloped, the crystallization of a protein is mainly a trial-and-error procedure, see, for example, Jan Drenth ("Principles of Protein X-ray Crystallography", pages 1-9).

In response, applicants traverse the Examiner's rejection. However, without conceding the correctness of the Examiner's position and in order to expedite prosecution, applicants have amended claim 48 (from which claims 21-22, 26-27, and 50-51 depend). Applicants note that the subject matter of claim 48, as amended, is indicated to be enabled by the Examiner in the March 14, 2003 Final Office Action. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claims Rejected Under 37 C.F.R. §112 - Second Paragraph

The Examiner stated that claims 21-22, 26-27, and 48-51 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the

invention. The Examiner stated that the phrase "the 3-D structure shape complementary or estimated interaction energy" is nowhere cited earlier in the claim. The Examiner stated that claims 21-22, 26-27, and 49-51 are rejected due to their dependency from claim 48.

In response, without conceding the correctness of the Examiner's position and in order to expedite prosecution, applicants have amended claim 48 to particularly point out and more distinctly claim the subject matter. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claims Rejected Under 37 C.F.R. §103(a)

The Examiner stated that claim 48 is rejected under 35 U.S.C. §103(a) as being unpatentable over Mohammadi et al., WO 98/07835. The Examiner stated that the claims are drawn to a method of performing a computer analysis of using the structural coordinates to identify an agent that potentially binds to Kit protein. The Examiner further stated that in addition to disclosing making a crystal and determining the structure of a protein tyrosine kinase, Mohammadi et al. shows in the abstract and throughout a method of performing a computer analysis of using the structural coordinates of the protein kinase to identify an agent that binds to and modulates the protein tyrosine kinase. The Examiner stated that such a modulator can activate or inhibit the catalytic activity of the protein tyrosine kinase, and that Mohammadi also discloses that these modulators are identified by a docking representation of a structure of a protein tyrosine kinase with or without a compound binding to it, which structure is defined by structural

coordinates. The Examiner stated that the computational process of identifying modulators by Mohammadi et al. differs from the claimed invention only in the content of the crystal coordinates. The Examiner stated that the difference between Mohammadi et al. and the claimed invention constitutes non-functional descriptive material because the content of the structure coordinates of a protein or protein complex does not alter how the computational method functions, i.e., the structural coordinates of the protein does not limit the claimed method to perform different steps than the method of Mohammadi et al. The Examiner stated that, therefore, no patentable weight is given to the structural coordinates of the protein in the claimed method.

In response, applicants traverse the Examiner's rejection. Applicants note that, as quoted by the Examiner, factors and considerations dictated by law governing 35 U.S.C. §103 apply without modification to computer-related inventions. Accordingly, all claim limitations must be taught or suggested by the alleged prior art. In addition, applicants note, as quoted by the Examiner in the March 14, 2003 Final Office Action, "Nonfunctional descriptive material cannot render nonobvious an invention that would have otherwise been obvious" MPEP §2106. Applicants maintain, however, that the claimed invention is not otherwise obvious. For example, applicants note that a fragment of SCF is neither taught nor suggested by the cited reference. Moreover, applicants note that a fragment of SCF consisting of amino acids having the sequence set forth in SEQ ID NO:1, as recited in claim 48, is neither taught nor suggested by the cited reference. Thus, the cited reference cannot support a *prima facie* case of obviousness. Accordingly, applicants respectfully request that the Examiner, reconsider

and withdraw this ground of rejection.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any such fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450 Alexandria, VA 22313-1450

6/12/03

John P. White Date
Registration No. 28,678

Mark-Up Copy of the Amendments to the Claims

Claim 48 has been amended as follows:

--48. A method for designing a compound capable of binding to the Stem Cell Factor-binding site of a Kit receptor comprising the steps of:

a) determining the 3-D structure of a fragment of Stem Cell Factor (SCF) by computing atomic co-ordinates from X-ray diffraction data of a crystal of the fragment of SCF [, wherein the fragment of SCF is capable of binding to the Kit] which consists of consecutive amino acids the sequence of which is set forth in SEQ ID NO:1;

b) determining a Kit receptor binding site on the fragment of SCF based on the 3-D structure; and

c) designing a compound capable of binding to the Stem Cell Factor-binding site of the Kit receptor based on a [the] 3-D structure shape complementarity or estimated interaction energy.--